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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,486	01/11/2002	Roger Y. Tsien	REGEN1510-1	9885

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EXAMINER

BERCH, MARK L

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/044,486

Applicant(s)

TSIEN ET AL.

Examiner

Mark L. Berch

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11-19-2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 5-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11-2003.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Quante.

See the species in patent claims 3-4, which correspond to R = thienylmethyl. The indole of claim 3, and the coumarin of claim 4 are taught by the reference to be fluorescent, and at any rate are extremely similar to the (III) and (IX) choices of claim 2 in this case, differing primarily in the exact nature of the linker. The traverse is unpersuasive. Applicants state that these compounds do not meet the requirement for the fluorescent moiety but do not explain why not. Paragraph 0032 says, "Suitable donor fluorogenic molecules include, but are not limited to, coumarins and related dyes....." These prior art compounds have a coumarin. The actual claim limitation is met.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. In (VII), does Me stand for metal or methyl? Either is conventional. For whichever choice is made, applicants must show that one of ordinary skill in the art would have known that this choice, and not another, was intended. The traverse is unpersuasive. It is true that M is used for metal, but Me is used for metal as well. See for example 3991051, Column 3, line 45; 3891635, column 1, lines 30-31; 4177189, abstract column 2, second line. Hundreds of other examples could be given; Me is routinely used for metal.
2. The term "ammonium cations" in claim 1 is unclear. Why is this in the plural – there should only be one. Further, is this just NH_4^+ , or is a substituted ammonium cation contemplated, and if so, substituted with what? The traverse is unpersuasive. Applicants have not explained why this is in the plural, when there is only one, and all the other choices, e.g. alkyl, are in the singular. Also, applicants have given no explanations to why the term would be understood as covering R as only H or alkyl, but not e.g. substituted alkyl, or phenyl, etc.
3. The term "acyl" (in acyloxy and acylthio) is indefinite. Does this embrace acids of S? P? As? What does the stem look like, i.e. if the acyl is e.g. RC(O) , what is R? The traverse is unpersuasive and in fact makes no sense at all. Applicants state, "an acylthiomethyl group has the structure RC(S) , wherein R is methyl". This is entirely mistaken. An acylthiomethyl group has the structure Acyl-S-CH_2- . The methyl is not part of the acyl group.

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4. The R3 definition in claim 2 is indefinite. The term “linker” does not convey what it is, only what the unknown group is attached to. The traverse is unpersuasive. Applicants state that the term is “defined” in paragraph 0046. This is not true. Paragraph 0046 states, “Suitable linkers for use as R3 include, but are not limited to, a direct bond to a heteroatom” That is clearly a list of examples, not a definition. The fact that it is “not limited to” that list means that some other, unknown choices are included.

Claims 2 and 3 are rejected under 35 U.S.C. 112, paragraphs 1 and 2, as the claimed invention is not described, or is not described in such full, clear, and exact terms as to enable any person skilled in the art to make and use the same, and/or failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. Specifically:

The formula (V) is depicted in claim 2 as having three minus charges but no plus charge. A molecule without electrical neutrality is impossible to prepare and hence lacks enablement in terms of how to make, as such a thing cannot be made (paragraph 1). Note MPEP 2172.01: “A claim which omits matter disclosed to be essential to the invention as described in the specification or in other statements of record may be rejected under 35 U.S.C. 112, first paragraph, as not enabling. *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). See also MPEP § 2164.08(c). Such essential matter may include missing elements ...”. Here, the missing counterion is the missing element. On the other hand, if it was not the intention of applicants to claim such a non-neutral molecule, then the claim fails to set forth what applicants intend as their invention (paragraph 2). That is, it is not accurate because it is missing something. As stated in *In*

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re Zletz, 13 USPQ2d 1320, 1322, "An essential purpose of patent examination is to fashion claims that are precise, clear, correct and unambiguous." Similarly in claim 3, one of the linkers (third line, 4th choice) has a plus charge but no balancing minus charge. The traverse is unpersuasive. The new structure (V) is the same as the old one, just drawn larger. No change was made to claim 3.

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to teach how to use this compound. It does not fall within the ambit of Formula I, to which utility is tied. Compounds of Formula I have a CH₂ group attached to the cephalosporin, and to which Z is attached via a single bond. This species meets neither requirement. It has a CH group, not a CH₂ group, and Z is attached via a double bond, not a single bond. There being no other place in the specification which teaches the utility for this compound, it lacks an ascribed utility, and hence is not enabled. The traverse is unpersuasive. Applicants have misunderstood the rejection. It is agreed that the compound is described in the specification, but that was not the issue here. The problem is that the specification fails to teach how to use this compound, since it does not fall within the ambit of Formula I, to which utility is tied.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

1. The $n = 1-4$ material appears to be new matter. It does not appear in paragraphs 0012 or 0046 or anywhere else the examiner could find. Applicants state, "Lower alkylene is defined in the specification at page 9, paragraph (0036) as a moiety containing 1-4 carbon atoms." This is entirely mistaken. The term "alkylene" never appears in that paragraph. Further, even if it did, the term under discussion is not "alkylene". What appears in that paragraph is discussion of a "membrane permeable derivative", a derivative of a free OH group somewhere in the molecule, a derivative which could have a substituent which ends in "alk" and then a definition is given for the terminal "alk". It is totally unrelated to this group, which is linking group within an ester group R'.

2. The use of the R' variable in the revised version of (VI) is clearly new matter.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.



Mark L. Berch
Primary Examiner
Art Unit 1624

January 8, 2004